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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,009	09/24/2003	Daniel J. Cosgrove	P04666US08	4403

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EXAMINER	
SAIDHA, TEKCHAND	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/670,009	COSGROVE ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 8 & 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL REJECTION

1. Applicants' Amendment and response filed June 23, 2006 is acknowledged. Claims 1-4, 8 & 12 are under consideration in this application.

2. Claims 5-7, 9-11 & 13-22 are and/or remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed.

3. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed as per the amendment cited above have been fully considered but they are not deemed to be persuasive. The reasons are discussed following the rejection(s).

5. Claims 8 & 12 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claims 8 & 12 depend from non-elected claims 5 & 11 respectively. Amending the claims to proper dependent form is required.

Applicants argue that although 37 CFR 1.75(c) requires the dependent claim to further limit a preceding claim, this rule does not apply to product-by-process claims.

Applicants' argument is considered but not found to be persuasive because the preceding claim(s) is a non-elected

claim(s). Adding the process steps into the product-by-process claims will overcome this rejection.

6. New matter added only to the claims - rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(a) Claim 8 depends upon claim 5, and claim 5 (line 3) recites new matter as follows: '8-30 contiguous bases', however, there is disclosure or support to this recitation in the application as originally filed. Applicants' published application US 20050272041 A1, paragraph 007, claims 5 & 9 disclose the range 4-30 contiguous nucleotides. Applicants are required to cancel the new matter in response to this rejection.

Applicants are also cautioned about the presence of this range, i.e., '8-30 contiguous bases', in the newly added claims which are not under consideration, but will be treated as new matter, as and when considered.

(b) Claim 8 depends upon claim 5, and claim 5 (lines 4-6) recites new matter as follows:

Lines 4-6 of claim 5, recites *"wherein a nucleotide sequence of said oligonucleotide is obtained by: aligning two or more nucleotide sequences of expansins according to sequence identity to identify a conserved sequence in said expansin sequences;"*. There is no basis for these method steps in the specification as originally filled. Applicants are required to cancel the new matter in response to this rejection.

7. Claims 2-3, 8 & 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: 'A polynucleotide sequence encoding an expansin protein wherein the polynucleotide sequence hybridizes under high stringency conditions (6X SSC, 50% formamide .....65°C for 15 min) to the sequence of SEQ ID NO: 1 or a method for identifying a nucleic acid sequence which encodes a protein with expansin activity, comprising the steps of isolating the nucleic acid sequence from a cDNA library by hybridization (under defined stringency conditions) using a DNA probe comprising the sequence of SEQ ID NO : 1', does not reasonably provide enablement for a polynucleotide that is at least 90% identical to the sequence of SEQ ID NO: 1 (claim 2) or a polynucleotide that encodes a polypeptide having at least 90% sequence identity to the sequences of SEQ ID Nos. 2-7 (claim 3); or method of identifying a nucleic acid comprising 'a oligonucleotide probe of 4-30 contiguous bases of SEQ ID NO : 1 (claim 8), or by using a undefined primer of clam 12.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988))[*Ex parte* Forman [230 USPQ 546 (Bd. Pat. App. & Int. 1986)]. The Wands factors are: (a) the quantity of experimentation necessary, (b)

the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim. The factors most relevant to this rejection are the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

The claim is drawn to encompass 'polynucleotide molecules' or method of identifying a polynucleotide encoding expansin using 'an oligonucleotide of any size ' ..of SEQ ID NO: 1 or fragment of undefined size for a 'PCR primer' or a 'hybridization probe' or obtaining cDNA of varying homology and which encodes amino acid sequences of SEQ ID NO : 2-6 of varying homology (90%) or designing a primer based upon the amino acid sequence of SEQ ID NO : 7. The specification, however, only discloses a single polynucleotide encoding a cucumber cEx-29. In addition the specification teaches the amino acid sequences (SEQ ID Nos. 2-7) of expansins from rice and *Arabidopsis*. Expansins are a new class of proteins that have been identified to be involved in cell wall expansion. Recent studies [Shcherban et. al, PNAS (1995, Sep 26), 92 (20): 9245-9, not prior art] have identified 4 distinct expansins cDNA in rice and at least 6 in Arabidopsis and show that the expansins from among these plant species, are highly conserved in size and sequence similarity (60-87 % amino acid sequence identity). Searching for sequence homology and comparison of amino acid sequence homology of expansin from Strawberry (AC : W81347), for example, and Applicants' amino acid sequence from Arabidopsis expansin (SEQ ID NO. 5) show a sequence homology of about 48.9%; and a

nucleotide sequence homology of 25% between Applicants' SEQ ID NO : 1 (cucumber expansin cDNA, AC : T13320) and the nucleotide sequence of strawberry expansin (AC : V68447). Such a low nucleotide sequence homology is insufficient to use the Applicants' SEQ ID NO: 1 as a probe (much less for a sequence that is 4-30 nucleotides in length or 90% similar to SEQ ID NO: 1 or a DNA that encodes sequences that are 90% similar to the amino acid sequences of SEQ ID Nos. 2-7) in order to clone the expansin polynucleotide from strawberry, even under high stringency conditions. So, if one skilled in the art were to use a fragment of SEQ ID NO: 1 as probe in order to clone similar genes, based upon the homology factor discussed above, the chances of successful hybridization are extremely low, in view of the unpredictable nature of the art, as well as inadequate guidance provided in the specification.

With regard to method claims 8 & 12 (depends upon non-elected claims 5 & 11 respectively) nucleic acid hybridization or amplification assays are extremely sensitive to the conditions in which they are performed. The buffer composition, pH, temperature, length of time, salt concentrations, quality and source of template nucleic acid, are all variables which determine the reproducibility of a given hybridization experiment. Given the unpredictability of the art and the nature of hybridization experiments in general, it is not sufficient to merely cite hybridization without a clear and explicit recitation of the conditions associated with the hybridization. For example, the definition of stringency as it pertains to hybridization conditions is subject to interpretation and is different from laboratory to laboratory. Therefore, without a clear and explicit recitation of the

conditions which were actually used by Applicants in isolating the claimed polynucleotides which hybridize to the disclosed sequences, the skilled artisan would not be able to practice the claimed invention and would not be reasonably apprised of the metes and bounds of the claimed invention. Without such guidance, the experimentation left to those skilled in the art is undue.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims 2 & 3 reciting 90% sequence identity, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of any expansin with 90% identity to the enzymes of SEQ ID NOS: 2-7, or the encoding DNA, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting expansin activity; (B) the general tolerance of expansin to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any expansin residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including DNA encoding expansin, or biological activity which may include activities other than expansin as none is described, with an enormous number of amino acid modifications of the of SEQ ID NOS: 2-7. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of expansin having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue in using the modified enzyme or DNA in the method claimed. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants' arguments regarding enablement and written description:

The written description rejection is withdrawn in view of claim amendment and Applicants' arguments.

Applicants argue (enablement rejection) that it is impermissible to use a later factual reference to determine whether the application is enabled or described as required under 35 U.S.C. 112, first paragraph. In re Koller, 613 F.2d 819, 823 n. 5, 204 USPQ 702, 706 n.5 (CCPA 1980).

In response it is pointed out the references used here which do not qualify as prior art because they postdate the claimed invention is relied upon to show the level of ordinary skill in the art at or around the time the invention was made. Ex parte Erlich, 22 USPQ 1463 (Bd. Pat. App. & Inter. 1992).

There is no bar against the use of such references (*see* MPEP § 2124). Therefore, the use of Shcherban reference is proper.

Applicants argue that even if the Shcherban reference is proper, the Examiner has not shown that the sequences with sequence similarity to Applicants' do not behave as expansin. Applicants have provided ample guidance for the methods claimed to allow one skilled in the art to make and use the invention described in the claims without undue experimentation. Applicants submit that the Examiner has ignored the Specification's teachings and failed to make a *prima facie* case of non-enablement. It should be noted that "A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." MPEP § 2164.04.

Furthermore, "it is incumbent upon the Patent Office . . . to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." MPEP 2164.04. The rejection fails to satisfy this standard as it has provided no substantial reason to doubt the objective truth of the statements made by Applicants in its Specification as to the scope of the invention.

Applicants' argument are considered and found not to be persuasive for the following reasons:

Applicants have provided no guidance about modifying SEQ ID NO: 1 or any polynucleotide that will encode a polypeptide having 90% sequence identity and that retains expansin activity (not biological activity) as in the unmodified sequences of SEQ ID Nos. 2-7. This is because the specification does not support the broad scope of the claims which encompass all modifications of an expansin by 10% as related to SEQ ID NOS: 2-7, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting expansin activity; (B) the general tolerance of expansin to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any expansin residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Thus leading to high unpredictability.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Applicants further arguments that "it is well settled law that enablement is not precluded by the necessity for some experimentation. Moreover, enablement does not require that all

encompassed embodiments be operative but rather that one skilled in the art can identify operative embodiments be operative rather that one skilled in the art can identify operative embodiments without engaging in undue experimentation. MPEP § 2164.06. "The test is not merely quantitative, since a considerable amount of experimentation is possible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988)."

In an unpredictable art such as the instant one, one skilled in the art would be required to establish A-D (as explained above) and considerable amount of experimentation in order to optimize the system of modifying the expansins. Similarly, suitable guidance is lacking regarding designing primers and probes that detect expansins based upon the knowledge of one nucleic acid sequence of SEQ ID NO: 1 and the amino acid sequences of SEQ ID NOS: 2-7, as no guidance or specific example are provided.

Applicants' arguments that the published specification, at paragraph 196, describes the use of degenerate primers based on the N-terminal amino acid sequence from cucumber S2 expansin to detect S2 expansin cDNA, is further evidence that any fragment of SEQ ID NO: 1 cannot be randomly used for identifying conserved expansin sequence(s). The instant claims do not use any specific degenerate primers sequences, and broadly refer to fragment size ranging from 4-30 of the entire length of SEQ ID NO: 1.

Applicants direct Examiner's attention to US Patent No. 6,350,935 issued to Bennet. In particular, Example 1 in the '935 patent describes the isolation and identification of tomato

expansin by aligning deduced amino acid sequences of the nine expansins and identifying two conserved amino acid domains from the alignment, and designing degenerate primers based upon conserved regions and successfully amplifying expansin cDNA from tomato. However, no such examples are described in the instant specification. Further, the instant product by process claims 8 & 12 are so broad and do not recite specific primers, and one of skill in the art without the necessary guidance will not be make and use the product in the manner claimed. Therefore, the claims are not enabled and the rejection is maintained.

8. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 3 & 12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3, line 2, recites 'retains biological activity'. The claim is indefinite because it is not clear what activities are encompassed by the phrase biological activity. Expansin activity (or cell wall extension activity) is the only known activity described. Substituting 'retains biological activity' with 'retains expansin activity' will overcome this rejection.

Applicants argue to have adopted the Examiner's [suggested] language. However, claim 3, still recites 'biological activity' instead of 'expansin activity'. Therefore, the rejection is maintained.

Claim 12 depends on claim 11, and claim 11 recites 'designing a primer ...based upon SEQ ID NO: 7'. The sequence of SEQ ID NO: 7 is an amino acid sequence. The claim is indefinite because it is not clear how a primer which is a short, single-stranded RNA or DNA segment that functions as the starting point

for polymerization of nucleotides, is obtained from a polypeptide sequence of SEQ ID NO: 7, unless translated.

It is suggested to amend claim 12 (& claim 8) to an independent claim - and amend claim 12 - to recite 'designing a degenerate primer ...based upon the N-terminal amino acid sequence of SEQ ID NO: 7', to overcome this rejection.

9. ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(a) Claims 1-4, 8 & 12 rejected under the judicially created doctrine of double patenting over claims 1-3 of U. S. Patent No. 6,255,466 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: The patented claims 1-3 are species claims drawn to an isolated polynucleotide comprising a nucleotide sequence of SEQ ID NO: 1 (or a polynucleotide that 90% identical

to SEQ ID NO: 1) and which encodes a protein having expansin activity; or a polynucleotide encoding any of the polypeptide of SEQ ID Nos. 2-7 and having expansin activity. The instant claims 1-4, 8 & 12 are genus claims drawn to isolated polynucleotide comprising a nucleotide sequence of SEQ ID NO: 1 (or a polynucleotide that 90% identical to SEQ ID NO: 1) and which encodes a protein having expansin activity or biological activity, or are identified using primers or probes. Claims 1-4, 8 & 12 are broader than the patented claims 1-3. Claim 1-4, 8 & 12 include a genus of variant or diverse sequences as compared to narrower patented species claims. Since species anticipates genus, claims 1-4, 8 & 12 are anticipated by patented claims.

Applicant' arguments:

Applicants argue that a terminal disclaimer will be provided upon notification of the allowance of the pending claims. The rejection is therefore maintained until such time.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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